

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

REC'D 31 AUG 2005

PCT

PCT

To:

see form PCT/ISA/220

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/US2005/008519

International filing date (day/month/year)  
16.03.2005

Priority date (day/month/year)  
16.03.2004

International Patent Classification (IPC) or both national classification and IPC  
C07K14/16, A61P35/00, C12N15/62, A61P31/00

Applicant  
INLST INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized Officer

Renggli-Zulliger, N

Telephone No. +49 89 2399-7482



# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 51311-00008	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. PCT/US2005/008519	International filing date ( <i>day/month/year</i> ) 16 March 2005 (16.03.2005)	Priority date ( <i>day/month/year</i> ) 16 March 2004 (16.03.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant INIST INC.		

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 <i>bis</i> .1(a).																								
2.	<p>This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p>In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.</p>																								
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 20%;">Box No. I</td> <td style="width: 70%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
<input checked="" type="checkbox"/>	Box No. I	Basis of the report																							
<input type="checkbox"/>	Box No. II	Priority																							
<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability																							
<input type="checkbox"/>	Box No. IV	Lack of unity of invention																							
<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement																							
<input type="checkbox"/>	Box No. VI	Certain documents cited																							
<input type="checkbox"/>	Box No. VII	Certain defects in the international application																							
<input type="checkbox"/>	Box No. VIII	Certain observations on the international application																							
4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																								

<p style="text-align: center;">The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 338 82 70</p>	<p>Date of issuance of this report 20 September 2006 (20.09.2006)</p> <hr/> <p>Authorized officer</p> <p style="text-align: center; font-size: 1.2em;">Simin Baharlou</p> <p>e-mail: pt09@wipo.int</p>
--	--

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2005/008519

**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:  
☒ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material:  
☒ in written format  
☒ in computer readable form
  - c. time of filing/furnishing:  
☐ contained in the international application as filed.  
☐ filed together with the international application in computer readable form.  
☒ furnished subsequently to this Authority for the purposes of search.
3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2005/008519

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial  
applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 10-12

because:

- ☒ the said international application, or the said claims Nos. 10-12 (IA) relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form

- ☐ has not been furnished
- ☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2005/008519

---

**Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or  
Industrial applicability; citations and explanations supporting such statement**

---

**1. Statement**

Novelty (N)	Yes: Claims	6-8, 15-17
	No: Claims	1-5, 9-14
Inventive step (IS)	Yes: Claims	-
	No: Claims	1-17
Industrial applicability (IA)	Yes: Claims	1-9, 13-17
	No: Claims	-

**2. Citations and explanations**

**see separate sheet**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/008519

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 10-12 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

- D1: GIANNOULI C ET AL: "FUSION OF A TUMOUR-ASSOCIATED ANTIGEN TO HIV-1 TAT IMPROVES PROTEIN-BASED IMMUNOTHERAPY OF CANCER" ANTICANCER RESEARCH, HELENIC ANTICANCER INSTITUTE, ATHENS,, GR, vol. 23, no. 4, July 2003 (2003-07), pages 3523-3532, XP009031082 ISSN: 0250-7005
- D2: VOCERO-AKBANI A M ET AL: "Killing HIV-infected cells by transduction with an HIV protease-activated caspase-3 protein" NATURE MEDICINE, NATURE PUBLISHING, CO, US, vol. 5, no. 1, January 1999 (1999-01), pages 29-33, XP002228967 ISSN: 1078-8956
- D3: DARBINIAN NUNE ET AL: "Growth inhibition of glioblastoma cells by human Puralpha" JOURNAL OF CELLULAR PHYSIOLOGY, vol. 189, no. 3, December 2001 (2001-12), pages 334-340, XP009052328 ISSN: 0021-9541
- D4: US-B1-6 667 151 (COHEN DAVID I) 23 December 2003 (2003-12-23)
- D5: DATABASE EMBL [Online] 1 November 1998 (1998-11-01), PARK ET AL.: "Tat protein" retrieved from EBI accession no. UNIPROT Database accession no. 090291

*Novelty (Article 33(1) and (2) PCT)*

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/008519

1) D1 discloses a vaccine comprising a fusion protein made of an immunostimulatory tat fused to E7 of human papilloma virus HPV16 produced by recombinant technology (Figure 1) (abstract). Therefore, the subject-matter of claims 1, 2, 3, 5, 9, 10, 11, 13, 14 is not novel.

2) D2 discloses a vaccine composed of tat fused to Casp3 that is useful to treat HIV (Figure 1 and Abstract) rendering subject-matter of claims 1, 2, 3, 9, 10, 12, 13 and 14 not novel.

3) D3 discloses a fusion protein comprising a tat and an Puralpha fragment that suppress glioblastoma cell growth (Figure 3, Abstract). Therefore, the subject-matter of claims 1, 2, 4, 9, 10, 13 and 14 is not novel.

4) The cited prior art does not disclose a fusion protein made of an antigen coupled to tat, which is oxidised, modified at position 6, 10 and 14 (P->G) or comprising the SEQ. ID n°11. Therefore, the subject-matter of claims 6-8, 15-17 is novel.

*Inventive step (Article 33(1) and (3) PCT)*

5) D1 is considered as the closest prior art document and discloses a vaccine comprising an immunostimulatory tat coupled to E7 protein fragment. D2 and D3 would be equally suitable as closest prior art.

The difference between D1 and the present application is the use of a modified tat i.e. oxidised, modified in position 6, 10 and 14 (P->G) or comprising SEQ. ID n°11.

The problem can therefore be seen as the provision of an alternative vaccine comprising an immunogenic tat fused to an antigen.

The result is achieved in the present application (examples 3 and 4).

D4 discloses a lentivirus vaccine comprising an oxidised tat molecule that is used in co-immunisation with p24 and is able to elicit a good immune response (Table 2).

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/008519

In view of D4, the person skilled in the art trying would fuse the antigen to the oxidised tat in order to optimise the vaccine without undue burden and with a reasonable expectation of success.

Therefore, the subject-matter of claims 6 and 15 does not involve an inventive step in view of D1 and D4.

6) The tat sequence is known from D5 however inventive step for claims 7, 8, 16 and 17 would only be acknowledged if a special technical effect is achieved with these modified tat compared to the vaccines of the prior art comprising an unmodified tatt (D1-D3).

*Industrial applicability (Article 33(1) and (4) PCT)*

7) For the assessment of the present claims 10-12 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.